## Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

## **Listing of Claims:**

1. (Currently amended) A compound of the Formula Ia:

$$L$$
— $\left($ Aa— $Ww$ — $Yy$ — $D\right)_p$ 

or a pharmaceutically acceptable salt thereof, wherein,

L- is a Ligand unit;

-A- is a Stretcher unit;

a is 1;

each -W- is independently an Amino Acid unit;

-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

p ranges from 1 to about 20; and

-D is a Drug unit of the formula:

wherein, the wavy line indicates the point of attachment to the Spacer unit, and

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independently at each location:

R<sup>2</sup> is selected from the group consisting of -H and -C<sub>1</sub>-C<sub>8</sub> alkyl;

 $R^3$  is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -O-(C<sub>1</sub>-C<sub>8</sub> alkyl), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle);

R<sup>4</sup> is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -O-(C<sub>1</sub>-C<sub>8</sub> alkyl), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle) wherein; R<sup>5</sup> is selected from the group consisting of -H and -methyl; or R<sup>4</sup> and R<sup>5</sup> join and form a ring with the carbon atom to which they are attached and R<sup>4</sup> and R<sup>5</sup> have the formula -(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>- wherein; R<sup>a</sup> and R<sup>b</sup> are independently selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl and -C<sub>3</sub>-C<sub>8</sub> carbocycle and n is selected from the group consisting of 2, 3, 4, 5 and 6;

R<sup>6</sup> is selected from the group consisting of -H and -C<sub>1</sub>-C<sub>8</sub> alkyl;

 $R^7$  is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -O-(C<sub>1</sub>-C<sub>8</sub> alkyl), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle);

each R<sup>8</sup> is independently selected from the group consisting of -H, -OH, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle and -O-(C<sub>1</sub>-C<sub>8</sub> alkyl);

 $R^9$  is selected from the group consisting of -H and -C<sub>1</sub>-C<sub>8</sub> alkyl;  $R^{10}$  is selected from the group consisting of:

Z is -O-, -S-,-NH- or -N( $R^{14}$ )-;

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 $R^{11}$  is selected from the group consisting of -H, -OH, -NH<sub>2</sub>, -NHR<sup>14</sup>, -N(R<sup>14</sup>)<sub>2</sub>, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -O-(C<sub>1</sub>-C<sub>8</sub> alkyl), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle); or  $R^{11}$  is an oxygen atom which forms a carbonyl unit (C=O) with the carbon atom to which it is attached and a hydrogen atom on this carbon atom is replaced by one of the bonds in the (C=O) double bond;

each  $R^{12}$  is independently selected from the group consisting of -aryl and -C<sub>3</sub>-C<sub>8</sub> heterocycle;

 $R^{13}$  is selected from the group consisting of -H, -OH, -NH<sub>2</sub>, -NHR<sup>14</sup>, -N(R<sup>14</sup>)<sub>2</sub>, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -O-(C<sub>1</sub>-C<sub>8</sub> alkyl), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1-8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle); and

each R<sup>14</sup> is independently -H or -C<sub>1</sub>-C<sub>8</sub> alkyl.

2-6. (Canceled)

7. (Currently amended) A compound of the formula Ia:

$$L - \left( A_{\overline{a}} - W_{\overline{w}} - Y_{\overline{y}} - D \right)_p$$
Ia

or a pharmaceutically acceptable salt thereof, wherein,

L- is a Ligand unit;

-A- is a Stretcher unit;

a is 1;

each -W- is independently an Amino Acid unit;

-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

p ranges from 1 to about 20; and

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-D is a Drug unit having the structure:

or a pharmaceutically acceptable salt thereof,

wherein, the wavy line [is] <u>indicates</u> the point of attachment to the Spacer unit, and independently at each location:

R<sup>2</sup> is selected from the group consisting of -H and -methyl;

R<sup>3</sup> is selected from the group consisting of -H, -methyl, and -isopropyl;

R<sup>4</sup> is selected from the group consisting of -H and -methyl;

 $R^5$  is selected from the group consisting of -isopropyl, -isobutyl, -sec-butyl, - methyl and -t-butyl or  $R^4$  and  $R^5$  join[,] and form a ring with the carbon atom to which they are attached and  $R^4$  and  $R^5$  have the formula - $(CR^aR^b)_n$ - wherein;  $R^a$  and  $R^b$  are independently selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, and

-C<sub>3</sub>-C<sub>8</sub> carbocycle, and n is selected from the group consisting of 2, 3, 4, 5 and 6;

R<sup>6</sup> is selected from the group consisting of -H and -methyl;

each R<sup>8</sup> is independently selected from the group consisting of -OH, -methoxy

and -ethoxy;

 $R^{10}$  is selected from the group consisting of:

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$$\mathbb{R}^{24} \mathbb{O}$$
 and 
$$\mathbb{C} \mathbb{H}_3$$
 
$$\mathbb{C} \mathbb{H}_3$$

 $R^{24}$  is selected from the group consisting of H and -C(O) $R^{25}$ -; wherein  $R^{25}$  is selected from the group consisting of -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle);

Z is -O-, -NH-, -OC(O)-, -NHC(O)-, or -NR<sup>28</sup>C(O)-; where  $R^{28}$  is selected from the group consisting of -H and -C<sub>1</sub>-C<sub>8</sub> alkyl;

n is 0 or 1; and

 $R^{27}$  is selected from the group consisting of -H, -N<sub>3</sub>, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle) when n is 0; and  $R^{27}$  is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle) when n is 1.

- 8. (Canceled)
- 9. (Currently amended) [A]<u>The</u> compound or a pharmaceutically acceptable salt of the compound of claim 1 where<u>in</u> -D is a Drug unit having the structure:

$$H_3C$$
 $CH_3$ 
 $CH_3$ 

10-16. (Canceled)

- 17. (Currently amended) [A]<u>The</u> compound or a pharmaceutically acceptable salt of the compound of claim 1 or claim 7 wherein the Ligand unit is an antibody.
- 18. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 17 wherein the antibody is a monoclonal antibody.
- 19. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 18 wherein the monoclonal antibody specifically binds the CD30 antigen, the CD20 antigen, the Lewis X or Y antigen, the CD33 antigen, the CD38 antigen, the CEA antigen, the CD19 antigen, the CA15-3 antigen or the epidermal growth factor antigen.
- 20. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where<u>in</u> -Yy- is:

Q is selected from the group consisting of -C<sub>1</sub>-C<sub>8</sub> alkyl, -O-(C<sub>1</sub>-C<sub>8</sub> alkyl), -halogen, -nitro and -cyano; and

m is an integer ranging from 0-4, the amino terminus of -Yy- forming a bond with the Amino acid unit and the other terminus of -Yy- forming a bond with the Drug unit.

21. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein -A- is:

$$\xi = \int_{0}^{\infty} \int_{(CH_2)_rC(O)-\xi}^{O}$$

and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino Acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

22. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein -A- is:

and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino Acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

23. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein -A- is:

and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

24. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where<u>in</u> -A- is:

$$N-(CH_2CH_2O)_rCH_2C(O)-\frac{3}{2}$$

and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

25. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein -A- is:

and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

26. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein -A- is:

$$S^{2}$$
 $N$ 
 $N$ 
 $CH_{2}CH_{2}O)_{r}CH_{2}C(O)$ 

the carbonyl terminus of -A- forming a bond with the Amino acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

27. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 21 where <u>in</u> -A- is:

$$N-(CH_2)_5CO-\frac{3}{2}$$

the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

28. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 22 where <u>in</u> -A- is:

the carbonyl terminus of -A- forming a bond with the Amino acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

29. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 24 where <u>in</u> -A- is:

the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

30. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where  $\underline{in}$  -W<sub>w</sub>- is -Phenylalanine-Lysine-, the amino terminus of -W<sub>w</sub>- forming a bond with the Stretcher unit and the C- terminus of -W<sub>w</sub>-forming a bond with the Spacer unit.

31-43. (Canceled)

44. (Currently amended) A compound of the formula:

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$$R^{16} \xrightarrow[R^2]{} O \xrightarrow[R^4]{} R^5 \xrightarrow[R^6]{} R^8 \xrightarrow[R^8]{} O \xrightarrow[R^8]{} CH_3 \xrightarrow[R^9]{} R^{11} \xrightarrow[R^12]{}$$

or a pharmaceutically acceptable salt thereof;

wherein, independently at each location:

R<sup>2</sup> is selected from the group consisting of -H and -C<sub>1</sub>-C<sub>8</sub> alkyl;

R<sup>3</sup> is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub>

carbocycle, -O-( $C_1$ - $C_8$  alkoxy), -aryl, - $C_1$ - $C_8$  alkyl-aryl, - $C_1$ - $C_8$  alkyl-( $C_3$ - $C_8$  carbocycle), - $C_3$ - $C_8$  heterocycle and - $C_1$ - $C_8$  alkyl-( $C_3$ - $C_8$  heterocycle);

R<sup>4</sup> is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -O-(C<sub>1</sub>-C<sub>8</sub> alkoxy), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle) wherein; R<sup>5</sup> is selected from the group consisting of -H and -methyl; or R<sup>4</sup> and R<sup>5</sup> join and form a ring with the carbon atom to which they are attached and R<sup>4</sup> and R<sup>5</sup> have the formula: -(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>- wherein; R<sup>a</sup> and R<sup>b</sup> are independently selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl and -C<sub>3</sub>-C<sub>8</sub> carbocycle and n is selected from the group consisting of 2, 3, 4, 5 and 6;

R<sup>6</sup> is selected from the group consisting of -H and -C<sub>1</sub>-C<sub>8</sub> alkyl;

 $R^7$  is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -O-(C<sub>1</sub>-C<sub>8</sub> alkoxy), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle);

each  $R^8$  is independently selected from the group consisting of -H, -OH, - $C_1$ - $C_8$  alkyl, - $C_3$ - $C_8$  carbocycle and -O-( $C_1$ - $C_8$  alkoxy);

 $R^9$  is selected from the group consisting of -H and -C<sub>1</sub>-C<sub>8</sub> alkyl;

R<sup>11</sup> is selected from the group consisting of -H, -OH, -NH<sub>2</sub>, -NHR<sup>14</sup>, -

 $N(R^{14})_2$ ,  $-C_1-C_8$  alkyl,  $-C_3-C_8$  carbocycle,  $-O-(C_1-C_8$  alkyl), -aryl,  $-C_1-C_8$  alkyl-aryl,  $-C_1-C_8$ 

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 $(C_3-C_8 \text{ carbocycle})$ ,  $-C_3-C_8 \text{ heterocycle}$  and  $-C_1-C_8 \text{ alkyl-}(C_3-C_8 \text{ heterocycle})$ ; or  $R^{11}$  is an oxygen atom which forms a carbonyl unit (C=O) with the carbon atom to which it is attached and a hydrogen atom on this carbon atom is replaced by one of the bonds in the (C=O) double bond;

each R<sup>12</sup> is independently selected from the group consisting of -aryl and -

C<sub>3</sub>-C<sub>8</sub> heterocycle;

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R<sup>13</sup> is selected from the group consisting of -H, -OH, -NH<sub>2</sub>, -NHR<sup>14</sup>, -

 $N(R^{14})_2$ ,  $-C_1-C_8$  alkyl,  $-C_3-C_8$  carbocycle,  $-O-(C_1-C_8$  alkoxy), -aryl,  $-C_1-C_8$  alkyl-aryl,  $-C_1-C_8$  alkyl- $(C_3-C_8$  carbocycle),  $-C_3-C_8$  heterocycle and  $-C_1-C_8$  alkyl- $(C_3-C_8$  heterocycle);

each R<sup>14</sup> is independently -H or -C<sub>1</sub>-C<sub>8</sub> alkyl;

R<sup>16</sup> is A'a-Ww-Yy-

## wherein

each -W- is independently an Amino Acid unit;

-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

-A' is a Stretcher unit; and

a is 1.

45. (Currently amended) The compound of claim 44 having the structure:

or a pharmaceutically acceptable salt thereof.

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46. (Currently amended) The compound of claim 44 having the structure:

or a pharmaceutically acceptable salt thereof.

- 47. (Canceled)
- 48. (Currently amended) The compound of claim 44 having the structure:

or a pharmaceutically acceptable salt thereof.

49-51. (Canceled)

52. (Currently amended) The compound of claim 44 having the structure:

or a pharmaceutically acceptable salt thereof.

- 53. (Canceled)
- 54. (Currently amended) The compound of claim 128 having the structure:

or a pharmaceutically acceptable salt thereof.

- 55. (Canceled)
- 56. (Currently amended) The compound of claim 1 having the structure:

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or a pharmaceutically acceptable salt thereof.

57-58. (Canceled)

59. (Currently amended) The compound of claim 1 having the structure:

or a pharmaceutically acceptable salt thereof.

60-76. (Canceled)

77. (Currently amended) The compound of claim 1 having the formula:

or a pharmaceutically acceptable salt thereof, wherein L is a monoclonal antibody.

78. (Canceled)

79. (Previously presented) The compound of claim 54 or a pharmaceutically acceptable salt thereof, wherein L is a monoclonal antibody.

80-99. (Canceled)

100. (Previously presented) The compound or pharmaceutically acceptable salt thereof of claim 79 wherein L specifically binds the CD20 antigen.

101-103. (Canceled)

104. (Previously presented) The compound or pharmaceutically acceptable salt thereof of claim 77 wherein L specifically binds the CD20 antigen.

105-110. (Canceled)

111. (Previously presented) A composition comprising an effective amount of a compound or a pharmaceutically acceptable salt thereof of claim 1 or claim 7, and a pharmaceutically acceptable carrier or vehicle.

112-118. (Canceled)

119. (Previously presented) The compound or a pharmaceutically acceptable salt thereof of claim 1 in an isolated or a purified form.

120. (Canceled)

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121. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where  $\underline{in}$  -W<sub>w</sub>- is -valine-citrulline-, the amino terminus of -W<sub>w</sub>- forming a bond with the Stretcher unit, and the C- terminus of -W<sub>w</sub>- forming a bond with a the Spacer unit.

122. (Currently amended) The compound of claim 44 or a pharmaceutically acceptable salt of the compound of claim 44, wherein

-A' is selected from the group consisting of:

wherein

G is selected from the group consisting of -Cl, -Br, -I, -O-mesyl and -O-tosyl;

J is selected from the group consisting of -Cl, -Br, -I, -F, -OH, -O-N-succinimide, -O-(4-nitrophenyl), -O-pentafluorophenyl, -O-tetrafluorophenyl and -O-C(O)-OR<sup>18</sup>;

[a is 1;]

 $R^{17}$  is selected from the group consisting of  $-C_1-C_{10}$  alkylene-,  $-C_3-C_8$  carbocyclo-,  $-O_1-C_1-C_8$  alkoxy)-, -arylene-,  $-C_1-C_{10}$  alkylene-arylene-, -arylene- $-C_1-C_{10}$  alkylene-,  $-C_1-C_{10}$  alkylene-( $-C_3-C_8$  carbocyclo)-, -( $-C_3-C_8$  carbocyclo)- $-C_1-C_1$  alkylene-, - $-C_3-C_8$  heterocyclo-, - $-C_1-C_1$  alkylene-( $-C_3-C_8$  heterocyclo)-, -( $-C_3-C_8$  heterocyclo)- $-C_1-C_1$  alkylene-, -( $-C_1-C_1$  alkylene-, -( $-C_1-C_1$ ) alkylene-, -

r is an integer ranging from 1-10; and

 $R^{18}$  is  $-C_1-C_8$  alkyl or -aryl.

- 123. (Canceled)
- 124. (Previously presented) A composition comprising an effective amount of a compound or a pharmaceutically acceptable salt thereof of claim 79 and a pharmaceutically acceptable carrier or vehicle.
- 125. (Previously presented) A composition comprising an effective amount of a compound or a pharmaceutically acceptable salt thereof of claim 121 and a pharmaceutically acceptable carrier or vehicle.
- 126. (Previously presented) The compound or a pharmaceutically acceptable salt thereof of claim 79 in an isolated or a purified form.
- 127. (Previously presented) The compound or a pharmaceutically acceptable salt thereof of claim 121 in an isolated or a purified form.
- 128. (Previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein

-Aa-Ww-Yy- has the formula:

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$$\begin{array}{c|c}
H_2N & O \\
NH & NH
\end{array}$$

the succinimido terminus forming a bond with the Ligand unit and the other terminus forming a bond with the Drug unit.

129. (Previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 7 wherein

-Aa-Ww-Yy- has the formula:

the succinimido terminus forming a bond with the Ligand unit and the other terminus forming a bond with the Drug unit.

- 130. (Previously presented) The compound or a pharmaceutically acceptable salt of the compound of claims 128 or 129 wherein the ligand unit is a monoclonal antibody.
- 131. (Currently amended) The compound or pharmaceutically acceptable salt thereof of claim 1 where in  $R^{10}$  is

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132. (Currently amended) The compound or pharmaceutically acceptable salt thereof of claim 7 wherein  $R^{10}$  is:

- 133. (Previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 19 wherein the monoclonal antibody specifically binds the CD30 antigen.
- 134. (Previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 19 wherein the monoclonal antibody specifically binds the CD19 antigen.
- 135. (Previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 19 wherein the monoclonal antibody specifically binds the CD33 antigen.
- 136. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein -A<sub>a</sub>- is:

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wherein  $R^{17}$  is selected from the group consisting of  $-C_1-C_{10}$  alkylene,  $C_3-C_8$  carbocyclo-,  $-O-(C_1-C_8$  alkyl)-, -arylene-,  $-C_1-C_{10}$  alkylene-arylene-, -arylene- $C_1-C_{10}$  alkylene-,  $-C_1-C_{10}$  alkylene-( $C_3-C_8$  carbocyclo)-,  $-(C_3-C_8$  carbocyclo)- $-C_1-C_{10}$  alkylene-,  $-C_3-C_8$  heterocyclo-,  $-C_1-C_{10}$  alkylene-( $-C_3-C_8$  heterocyclo)-,  $-(C_3-C_8$  heterocyclo)- $-C_1-C_1$  alkylene-,  $-(C_1-C_1)$  alkylene-,  $-(C_1-C_1)$ 

- 137. (Currently amended) [A]<u>The</u> compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein p ranges from 1 to about 5.
- 138. (Currently amended) [A]<u>The</u> compound or a pharmaceutically acceptable salt of the compound of claim 79 wherein p ranges from 1 to about 5.
- 139. (Currently amended) [A]The compound or a pharmaceutically acceptable salt of the compound of claim 54 wherein L is a monoclonal antibody that specifically binds the CD30 antigen, the CD20 antigen, the Lewis X or Y antigen, the CD33 antigen, the CD19 antigen, the CD38 antigen, the CEA antigen, the CA15-3 antigen or the epidermal growth factor antigen.
- 140. (Currently amended) [A]<u>The</u> compound or a pharmaceutically acceptable salt of the compound of claim 139 wherein the monoclonal antibody specifically binds the CD30 antigen.
- 141. (Currently amended) A composition comprising drug-linker-ligand conjugates having Formula Ia:

$$L - \left( A_{\overline{a}} - W_{\overline{w}} - Y_{\overline{y}} - D \right)_{p}$$
Ia

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or a pharmaceutically acceptable salt thereof; wherein,

L- is a Ligand unit;

-A- is a Stretcher unit;

a is 1;

each -W- is independently an Amino Acid unit;

-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

p ranges from 1 to about 5 and is the average number of  $-A_a$ - $W_w$ - $Y_y$ -D units per ligand in the composition; and

-D is a Drug unit of the formula:

wherein, the wavy line indicates the point of attachment to the Spacer unit, and independently at each location:

 $R^2$  is selected from the group consisting of -H and -C<sub>1</sub>-C<sub>8</sub> alkyl;

 $R^3$  is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -O<sub>-</sub>(C<sub>1</sub>-C<sub>8</sub> alkyl), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle);

 $R^4$  is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, - O-(C<sub>1</sub>-C<sub>8</sub> alkyl), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle) wherein;  $R^5$  is selected from the group consisting of -H and -methyl; or  $R^4$  and  $R^5$  join and form a ring with the carbon atom to which they are attached and

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R<sup>4</sup> and R<sup>5</sup> have the formula -(CR<sup>a</sup>R<sup>b</sup>)<sub>n</sub>- wherein: R<sup>a</sup> and R<sup>b</sup> are independently selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl and -C<sub>3</sub>-C<sub>8</sub> carbocycle and n is selected from the group consisting of 2, 3, 4, 5 and 6;

R<sup>6</sup> is selected from the group consisting of -H and -C<sub>1</sub>-C<sub>8</sub> alkyl;

R<sup>7</sup> is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, - $O-(C_1-C_8 \text{ alkyl})$ , -aryl,

-C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle);

each R<sup>8</sup> is independently selected from the group consisting of -H, -OH, -C<sub>1</sub>-C<sub>8</sub> alkyl,  $-C_3-C_8$  carbocycle and  $-O-(C_1-C_8$  alkyl);

R<sup>9</sup> is selected from the group consisting of -H and -C<sub>1</sub>-C<sub>8</sub> alkyl;

R<sup>10</sup> is selected from the group consisting of:

$$R^{11} \longrightarrow R^{12}$$

$$Z \longrightarrow R^{12}$$
and
$$Z \longrightarrow R^{13}$$

Z is -O-, -S-,-NH- or -N( $R^{14}$ )-;

R<sup>11</sup> is selected from the group consisting of -H, -OH, -NH<sub>2</sub>, -NHR<sup>14</sup>, -N(R<sup>14</sup>)<sub>2</sub>, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -O-(C<sub>1</sub>-C<sub>8</sub> alkyl), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle); or R<sup>11</sup> is an oxygen atom which forms a carbonyl unit (C=O) with the carbon atom to which it is attached and a hydrogen atom on this carbon atom is replaced by one of the bonds in the (C=O) double bond;

each R<sup>12</sup> is independently selected from the group consisting of -aryl and -C<sub>3</sub>-C<sub>8</sub> heterocycle;

R<sup>13</sup> is selected from the group consisting of -H, -OH, -NH<sub>2</sub>, -NHR<sup>14</sup>, -N(R<sup>14</sup>)<sub>2</sub>, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -O-(C<sub>1</sub>-C<sub>8</sub> alkyl), -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1-8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle); and

each R<sup>14</sup> is independently -H or -C<sub>1</sub>-C<sub>8</sub> alkyl.

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Response to Notice of Allowance September 25, 2009

142. (Currently amended) A composition comprising drug-linker-ligand conjugates having Formula Ia:

$$L - \left( -A_{\overline{a}} - W_{\overline{w}} - Y_{\overline{y}} - D \right)_{p}$$
Ia

or a pharmaceutically acceptable salt thereof wherein,

L- is a Ligand unit;

-A- is a Stretcher unit;

a is 1;

each -W- is independently an Amino Acid unit;

-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

p ranges from 1 to about 5 and is the average number of - $A_a$ - $W_w$ - $Y_y$ -D units per ligand in the composition; and

-D is a Drug unit having the structure:

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or a pharmaceutically acceptable salt thereof,

wherein, the wavy line [is]indicates the point of attachment to the Spacer unit, and independently at each location:

R<sup>2</sup> is selected from the group consisting of -H and -methyl;

R<sup>3</sup> is selected from the group consisting of -H, -methyl, and -isopropyl;

R<sup>4</sup> is selected from the group consisting of -H and -methyl;

 $R^5$  is selected from the group consisting of -isopropyl, -isobutyl, -sec-butyl, - methyl and -t-butyl or  $R^4$  and  $R^5$  join[,] and form a ring with the carbon atom to which they are attached and  $R^4$  and  $R^5$  have the formula - $(CR^aR^b)_n$ - where in:  $R^a$  and  $R^b$  are independently selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, and

-C<sub>3</sub>-C<sub>8</sub> carbocycle, and n is selected from the group consisting of 2, 3, 4, 5 and 6;

 $R^6$  is selected from the group consisting of -H and -methyl;

each R<sup>8</sup> is independently selected from the group consisting of -OH, -methoxy

and -ethoxy;

R<sup>10</sup> is selected from the group consisting of:

$$R^{24}O$$
 and  $(Z)_nR^{27}$ 

 $R^{24}$  is selected from the group consisting of H and -C(O) $R^{25}$ -; wherein;  $R^{25}$  is selected from the group consisting of -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle);

 $Z \ is \ -O-, \ -NH-, \ -OC(O)-, \ -NHC(O)-, \ or \ -NR^{28}C(O)-; \ {\hbox{$where$};$} \ R^{28} \ is \ selected \ from$  the group consisting of -H and -C1-C8 alkyl;

n is 0 or 1; and

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 $R^{27}$  is selected from the group consisting of -H, -N<sub>3</sub>, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> carbocycle), -C<sub>3</sub>-C<sub>8</sub> heterocycle and -C<sub>1</sub>-C<sub>8</sub> alkyl-(C<sub>3</sub>-C<sub>8</sub> heterocycle) when n is 0; and

 $R^{27}$  is selected from the group consisting of -H, -C<sub>1</sub>-C<sub>8</sub> alkyl, -C<sub>3</sub>-C<sub>8</sub> carbocycle, -aryl, -C<sub>1</sub>-C<sub>8</sub> alkyl-aryl,

 $-C_1-C_8$  alkyl- $(C_3-C_8$  carbocycle),  $-C_3-C_8$  heterocycle and  $-C_1-C_8$  alkyl- $(C_3-C_8$  heterocycle) when n is 1.

143. (Currently amended) The composition of claim 141 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, R<sup>10</sup> is

144. (Currently amended) The composition of claim 142 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, R<sup>10</sup> is

145. (Currently amended) The composition of claim 141 where<u>in in the drug-linker-ligand conjugates or pharmaceutically acceptable salt thereof,</u> -D is a Drug unit having the structure:

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or a pharmaceutically acceptable salt thereof.

146. (Currently amended) The composition of claim 141 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, -Aa-Ww-Yy- has the formula:

the succinimido terminus forming a bond with the Ligand unit and the other terminus forming a bond with the Drug unit.

147. (Currently amended) The composition of claim 142 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, -Aa-Ww-Yy- has the formula:

$$\begin{array}{c|c}
H_2N & O \\
NH & O \\
NH & O \\
N & O \\
N & O \\
O & O \\$$

the succinimido terminus forming a bond with the Ligand unit and the other terminus forming a bond with the Drug unit.

- 148. (Currently amended) The composition of claim 141 where<u>in in the drug-linker-ligand conjugates or pharmaceutically acceptable salt thereof</u>, the ligand unit is a monoclonal antibody.
- linker-ligand conjugates or pharmaceutically acceptable salt thereof, the monoclonal antibody specifically binds the CD30 antigen, the CD20 antigen, the CD19 antigen, the Lewis X or Y antigen, the CD33 antigen, the CD38 antigen, the CEA antigen, the CA15-3 antigen or the epidermal growth factor antigen.
- 150. (Currently amended) The composition of 149 wherein <u>in the drug-linker-ligand conjugates or pharmaceutically acceptable salt thereof</u>, the monoclonal antibody specifically binds the CD19 antigen.
- 151. (Currently amended) The composition of claim 149 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, the monoclonal antibody specifically binds the CD30 antigen.
- 152. (Currently amended) The composition of claim 149 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, the monoclonal antibody specifically binds the CD33 antigen.

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153. (Currently amended) The composition of claim 147 wherein the drug-linker-ligand conjugates have the formula:

or a pharmaceutically acceptable salt thereof.

- 154. (Currently amended) The composition of claim 153 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, L is a monoclonal antibody.
- 155. (Currently amended) The composition of claim 154 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, the monoclonal antibody specifically binds the CD20 antigen, the CD30 antigen, the CD33 antigen, the CD19 antigen, the CD38 antigen, the CA15-3 antigen, the CEA antigen, or the epidermal growth factor antigen.
- 156. (Currently amended) The composition of claim 155 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, the monoclonal antibody specifically binds the the CD30 antigen.
- 157. (Currently amended) The composition of claim 155 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, the monoclonal antibody specifically binds the CD19 antigen.
- 158. (Currently amended) The composition of claim 155 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, the monoclonal antibody specifically binds the CD20 antigen.

159. (Currently amended) The composition of claim 155 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, the monoclonal antibody specifically binds the CD33 antigen.

- 160. (Currently amended) The composition of claim 142 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, L is a monoclonal antibody.
- linker-ligand conjugates or pharmaceutically acceptable salt thereof, the monoclonal antibody specifically binds the CD20 antigen, the CD30 antigen, the CD33 antigen, the CD19 antigen, the CD38 antigen, the CA15-3 antigen, the CEA antigen, or the epidermal growth factor antigen.
- 162. (Currently amended) The composition of claim 161 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, the monoclonal antibody specifically binds the CD30 antigen.
- 163. (Currently amended) The composition of claim 154 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, the antibody is attached to the drug moiety through a cysteine residue of the antibody.
- 164. (Currently amended) The compound of claim 122 or a pharmaceutically acceptable salt of the compound of claim 122, wherein

Aa- is:

wherein  $R^{17}$  is selected from the group consisting of  $-C_1-C_{10}$  alkylene,  $C_3-C_8$  carbocyclo-,  $-O-(C_1-C_8$  alkyl)-, -arylene-,  $-C_1-C_{10}$  alkylene-arylene-, -arylene- $C_1-C_{10}$  alkylene-,  $-C_3-C_8$  carbocyclo)-,  $-(C_3-C_8$  carbocyclo)- $-C_1-C_{10}$  alkylene-,  $-C_3-C_8$  heterocyclo-

- , -C<sub>1</sub>-C<sub>10</sub> alkylene-(C<sub>3</sub>-C<sub>8</sub> heterocyclo)-, (C<sub>3</sub>-C<sub>8</sub> heterocyclo)-C<sub>1</sub>-C<sub>10</sub>alkylene-, -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>r</sub>-, and -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>r</sub>-CH<sub>2</sub>-; and r is an integer ranging from 1-10.
- 165. (Currently amended) The compound of claim 1 or a pharmaceutically acceptable salt of the compound of claim 1 wherein  $R^2$  is  $-C_1-C_8$  alkyl.
- 166. (Currently amended) The composition of claim 141 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, R<sup>2</sup> is -C<sub>1</sub>-C<sub>8</sub> alkyl.
- 167. (Currently amended) The compound of claim 7 or a pharmaceutically acceptable salt of the compound of claim 7 wherein  $R^2$  is -methyl.
- 168. (Currently amended) The composition of claim 142 wherein in the druglinker-ligand conjugates or pharmaceutically acceptable salt thereof, R<sup>2</sup> is -methyl.